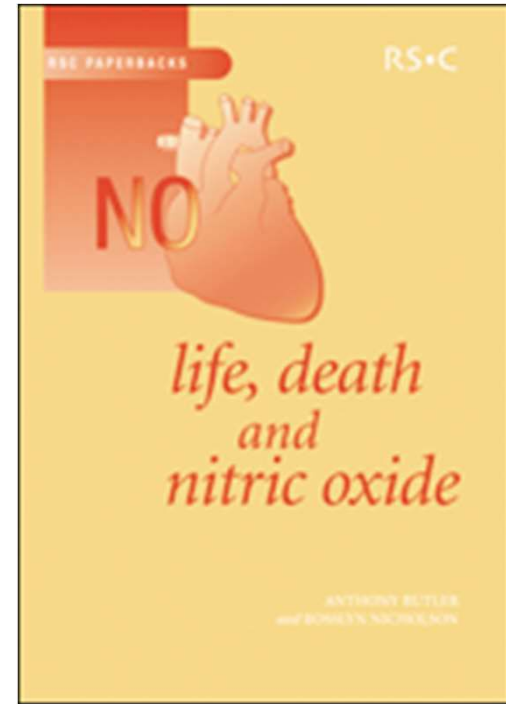


Arey PPHN!!! How to manage?



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Scenario.....

Labour and Delivery:

- Term infant, NVD, Thin MSL
- Vigorous at birth
- APGAR 8, 9

- At 1 hr nurse noted baby to be dusky, with rapid breathing

Vitals:

SpO ₂ 55% in room air	Temp 36.6 C
HR 146/min	CRT 5-6 sec
Faint murmur	MBP = 36 mmHg
Mod retractions	RR 60/min

SpO₂ -Pre69% & Post 50% in FiO₂ 100%



Scenario.....

Intervention:

Intubated [CMV 24/6,
50/m, Ti 0.35s]

FiO₂ 100%, SpO₂ 85 / 69%

Art Gas: 7.01/79/35/16/
-12



What are the differential ?



Sepsis and Shock



Congenital heart disease



MAS with PPHN



All of the above



None of the above

PPHN

Failure of normal postnatal adaptation with **persistent high PVR** (pulmonary vascular resistance) leading to --

- Right ventricular failure and
- Pulmonary ↔ systemic channel shunting

Pulmonary Hypertension

Reversible

Irreversible

Pulmonary

Non-pulmonary

Early

Late

RDS

TTN

MAS

Pneumonia

BPD

PIE

Hypoxia (HIE)

Vein of Galen

Pulmonary overcirculation

Neuromuscular

Drug (i.e. NSAID, SSRI)

Pulmonary hypoplasia

Alveolar capillary dysplasia

Pulmonary interstitial lymphangiectasia

Surfactant apoprotein B deficiency

Clinical assessment...

- Baby have respiratory distress
- Difference of 10-15 % in Pre and Post ductal SpO₂
- Hyperoxia test
- Hyperoxia Hyperventilation test
- Other predisposing factors
- Shock, poor perfusion

Clinical assessment **ALONE** does not allow accurate evaluation of the nature of the cardiovascular compromise

KANAGARAJAH
BABY GIRL
2172080

MI:1.1 TIS:2.0 S12 SONOS 5500
25 FEB 05 13:04:58 UNIT # 4
2/0/E/M2/C 7CM PAEDS HP 4
GAIN 50 COMP 41 20HZ

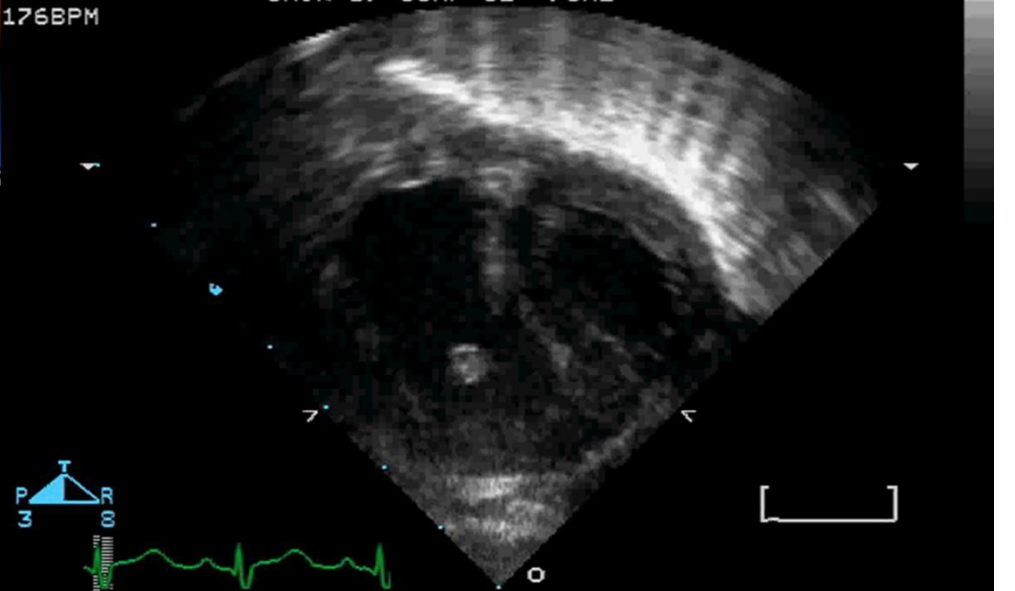
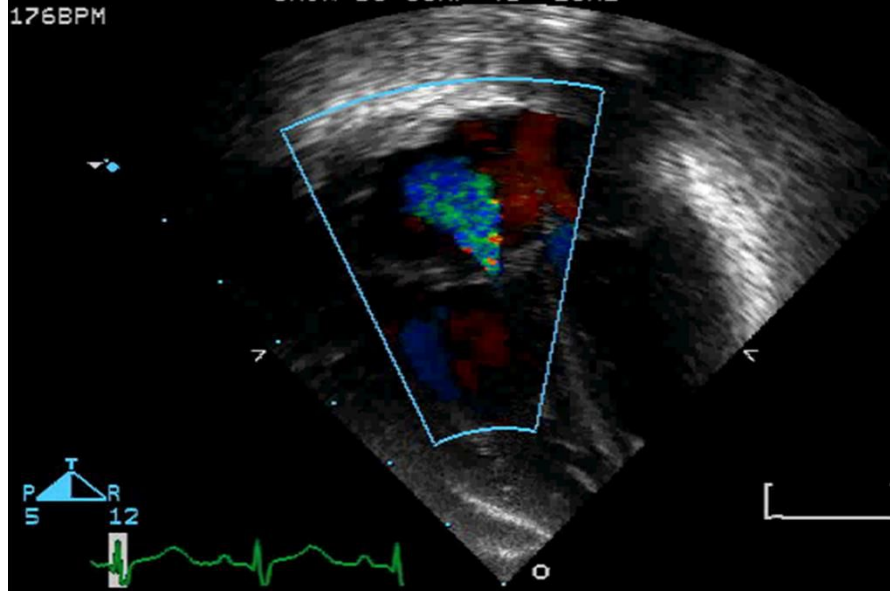
S.KANAGARAJAH
65BABY GIRL
2172080

MI:0.7 S8 SONOS 5500
25 FEB 05 13:11:12 UNIT # 4
2/0/E/F2 7CM PAEDS HP 4
GAIN 57 COMP 32 78HZ

176BPM

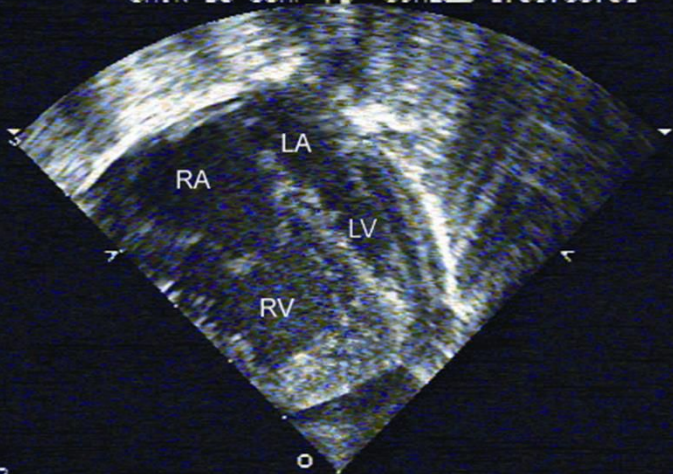
176BPM

C
M
S
65



MI:1.1 S12 Hospital For
10 MAY 04 17:13:26 Sick Children
2/0/E/F3 6CM HSC PED HP 4
GAIN 50 COMP 75 89HZ 1:03:33.01

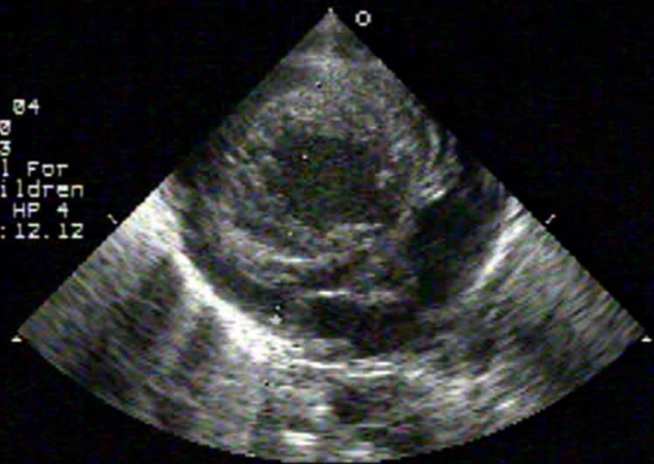
1598PM



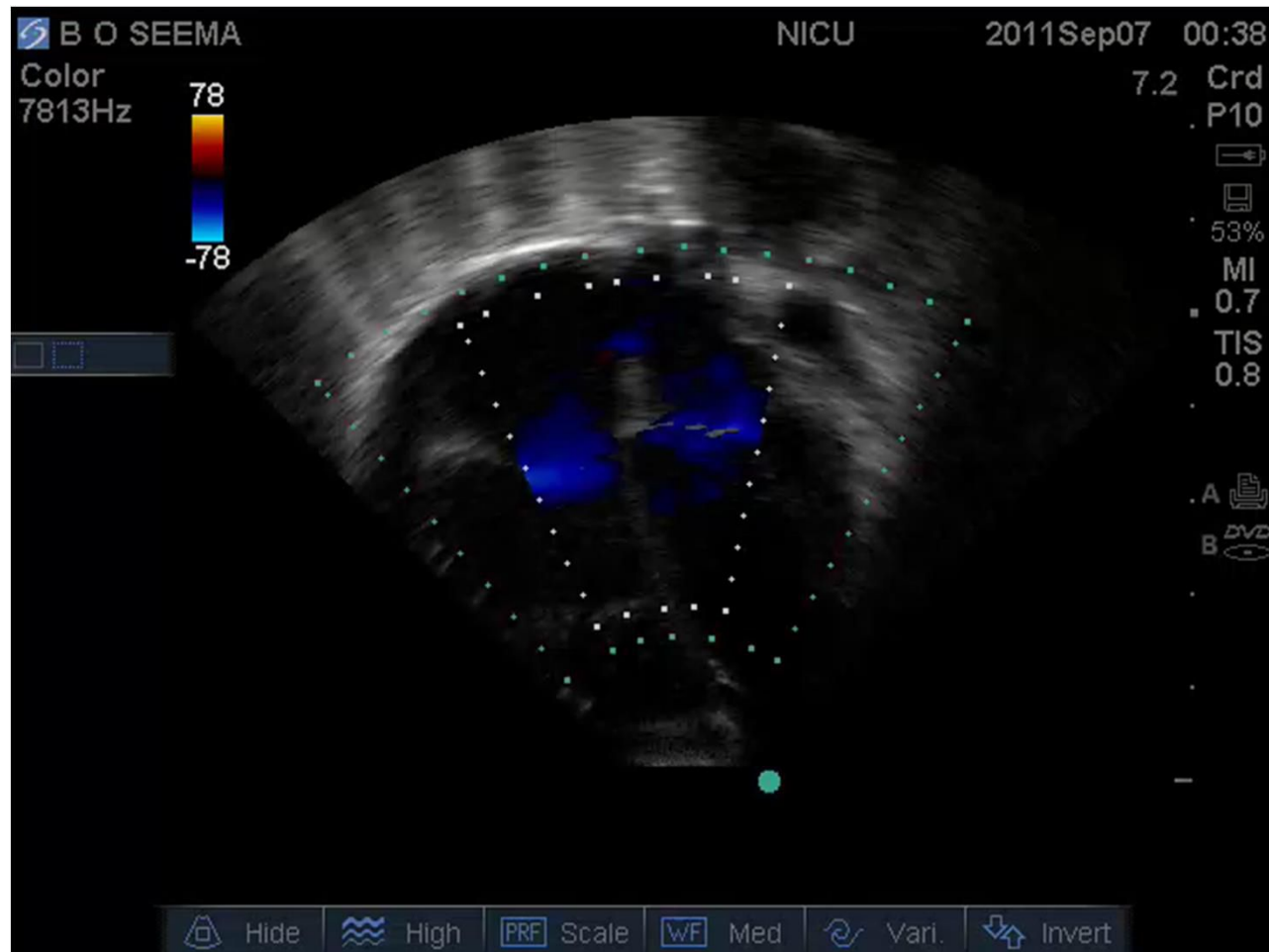
KWAN
LINDSAY
2137813

MI:1.1 S12
10 MAY 04 17:21:40
2/0/E/F3
Hospital For Sick Children
HSC PED HP 4
GAIN 50 COMP 75 89HZ
1536PM

6CM
89HZ



4Chamber colour doppler



B O BABU LAL

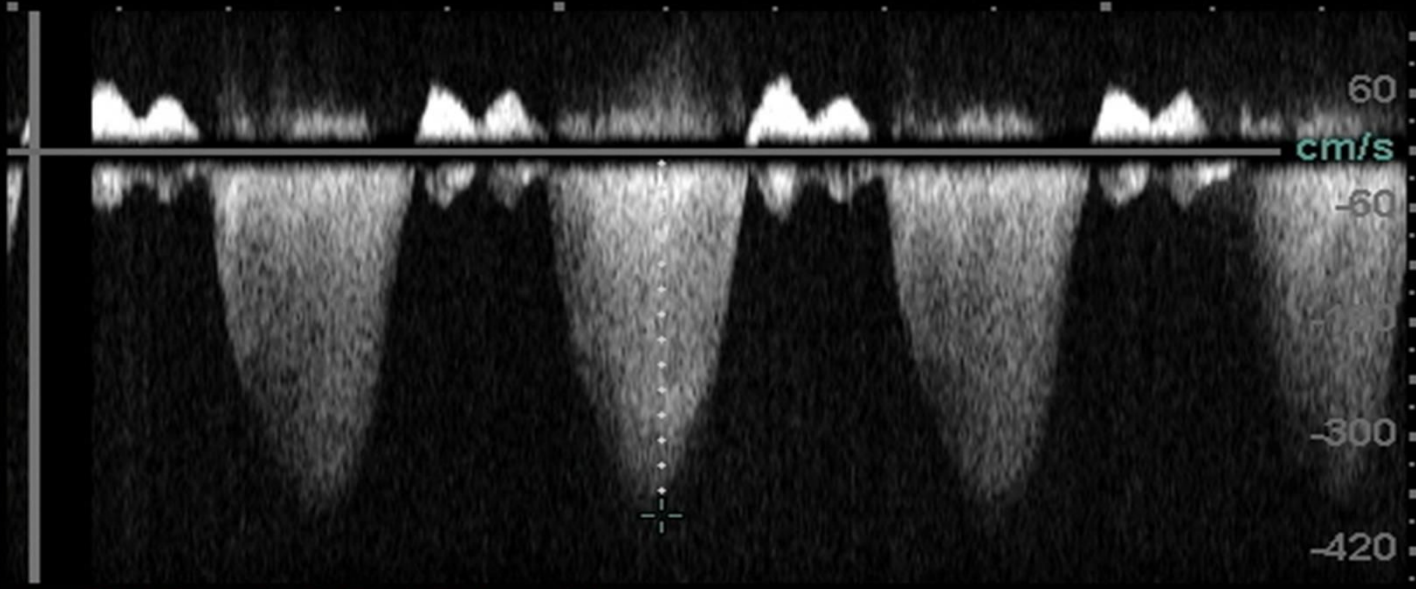
ASAKA.

2011 Sep 09 20:01

Color
7813Hz
CW
31250Hz



Crd
P10
52%
MI
0.0
TIS
0.6



A
B

Cine

A 382.2cm/s PGr:58.4mmHg

PHT Manual Auto Time Delete

Traditional teaching

- Oxygen vasodilator, keep SpO₂ 99-100, PaO₂ 80 or above
- Hyperventilate to
 - Alkalotic pH
 - Co₂ wash out
- Give Sodabcarb to achieve alkalosis
- Give Dopamine , Adrenalin to achieve suprasystemic Blood pressures

Physiologic Approach

Treat the problem not the consequences

- **Optimize lung recruitment**
- **Effective pulmonary vasodilation**
- **Achieve normal cardiac output and blood pressure**

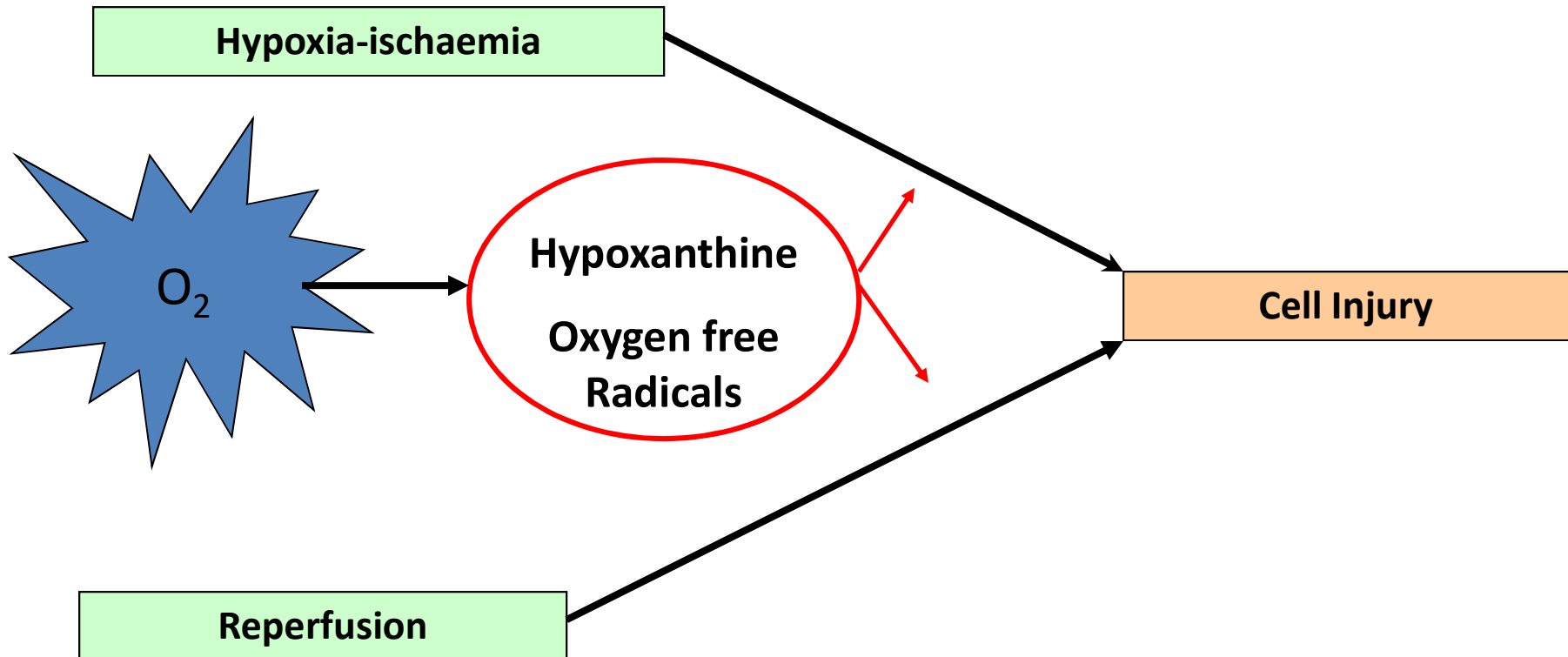
Ventilation

- Appropriate setting to minimize lung damage
 - Different modes (HFOV, HFJV)
 - Try to avoid high MAP – tend to change mode from conventional if
 - MAP 12 or more and FiO₂ > 60% to maintain SPO₂
 - OI are > 15
 - Measures to decrease PVR
 - Never hyperventilate

Oxygen & PPHN

- Pulmonary vasodilator
- paO_2 target range?
> 95% vs 90-85%
- Merits of post-ductal SpO_2 monitoring?

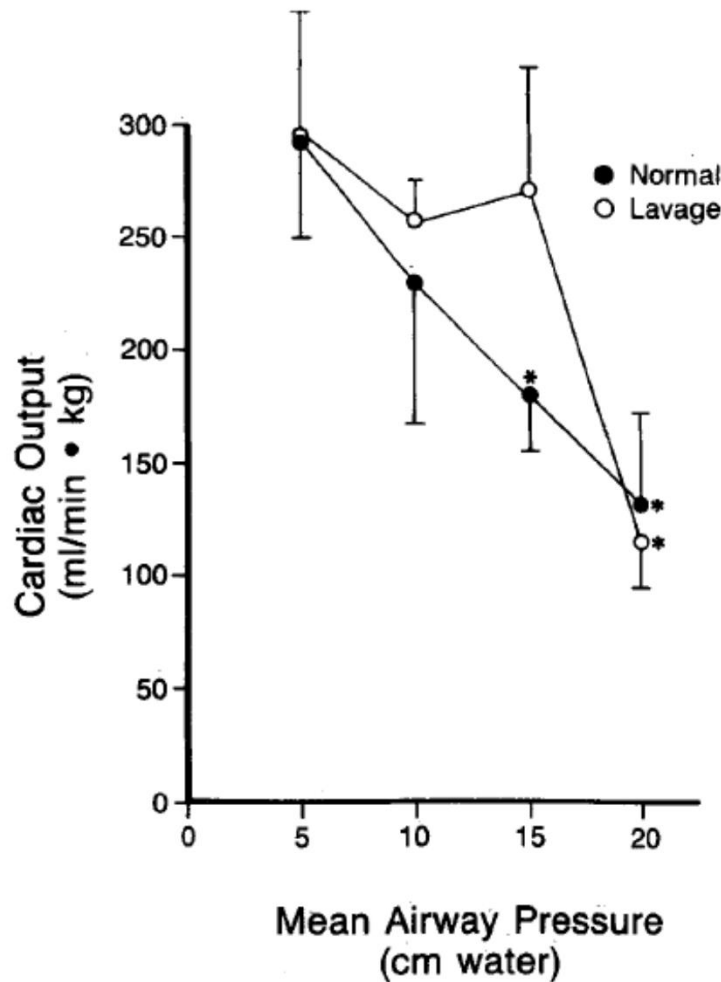
Oxygen Paradox



Oxygen Saturation Target

- Target pre-ductal SpO₂ [88-94%] and paO₂ [50-80 mmHg]
- No evidence to support SpO₂ > 95% or paO₂ > 80 mmHg
- Cautious approach to pre-post ductal gradient
(?? > 75% acceptable if lactate, pH, urinary output normal)

Mean Airway Pressure & Blood flow



Mirro 1987 J Pediatr

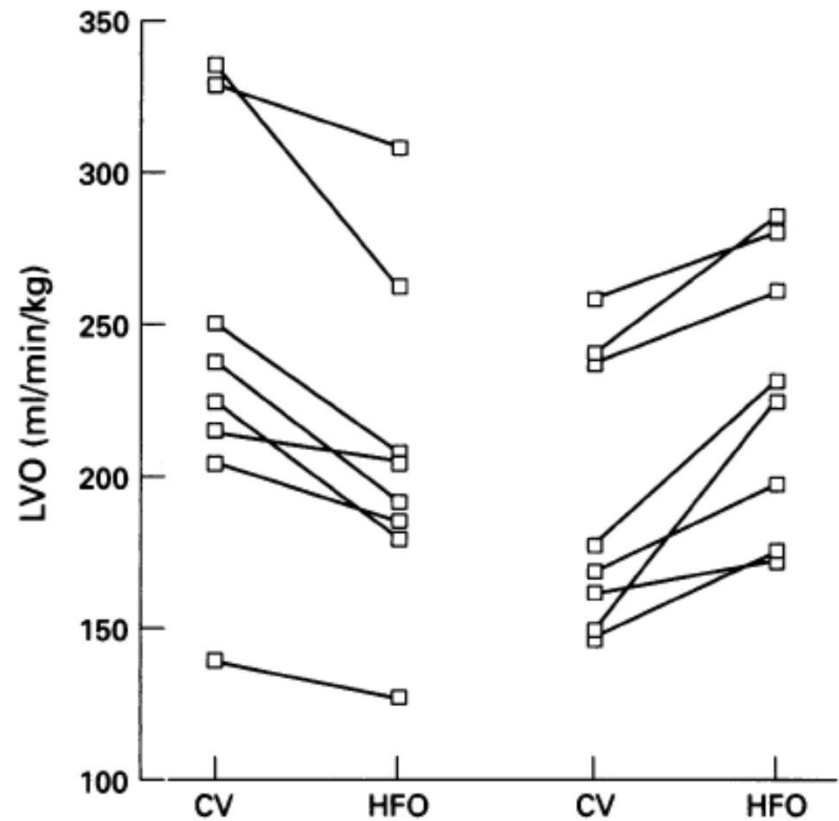
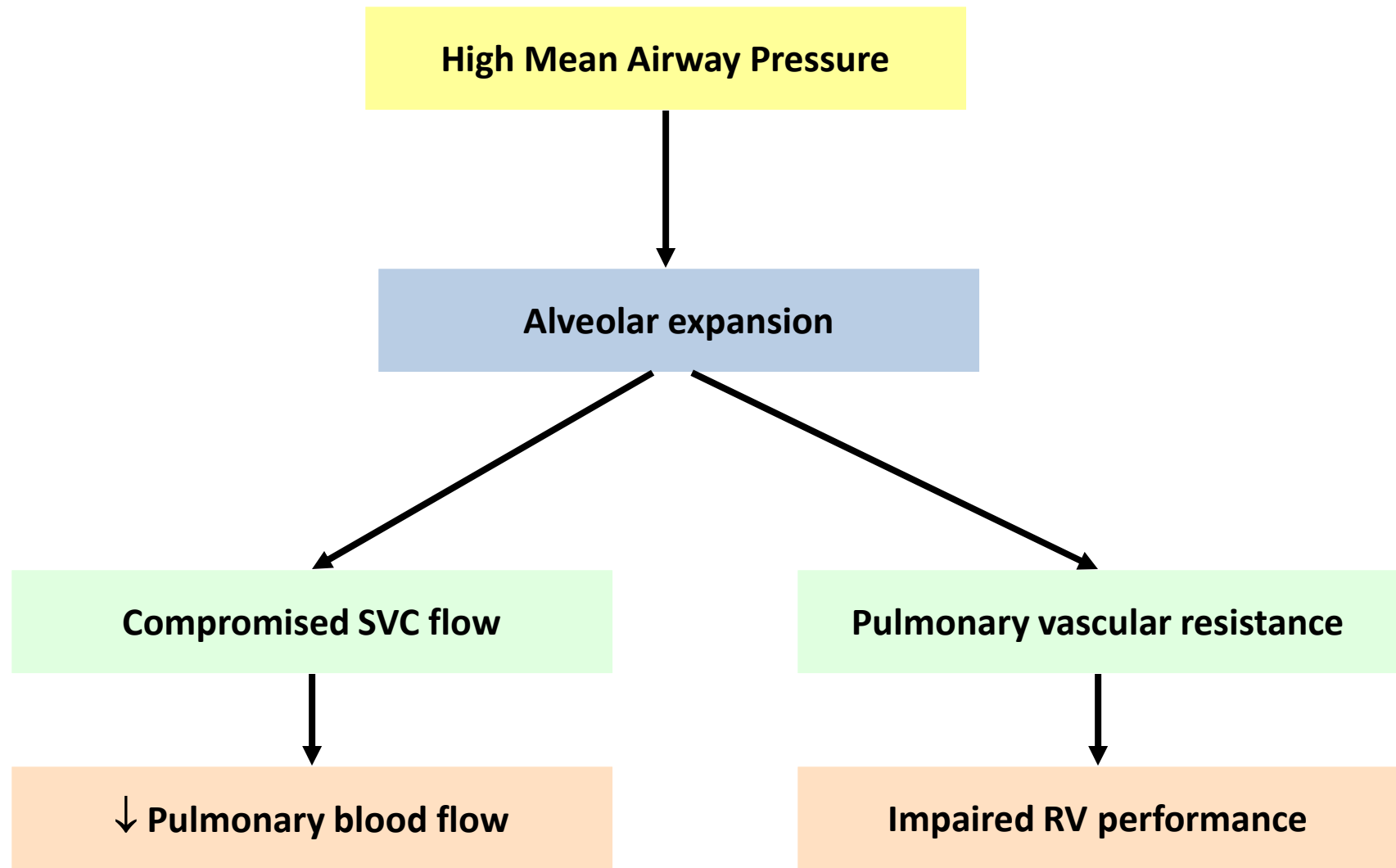


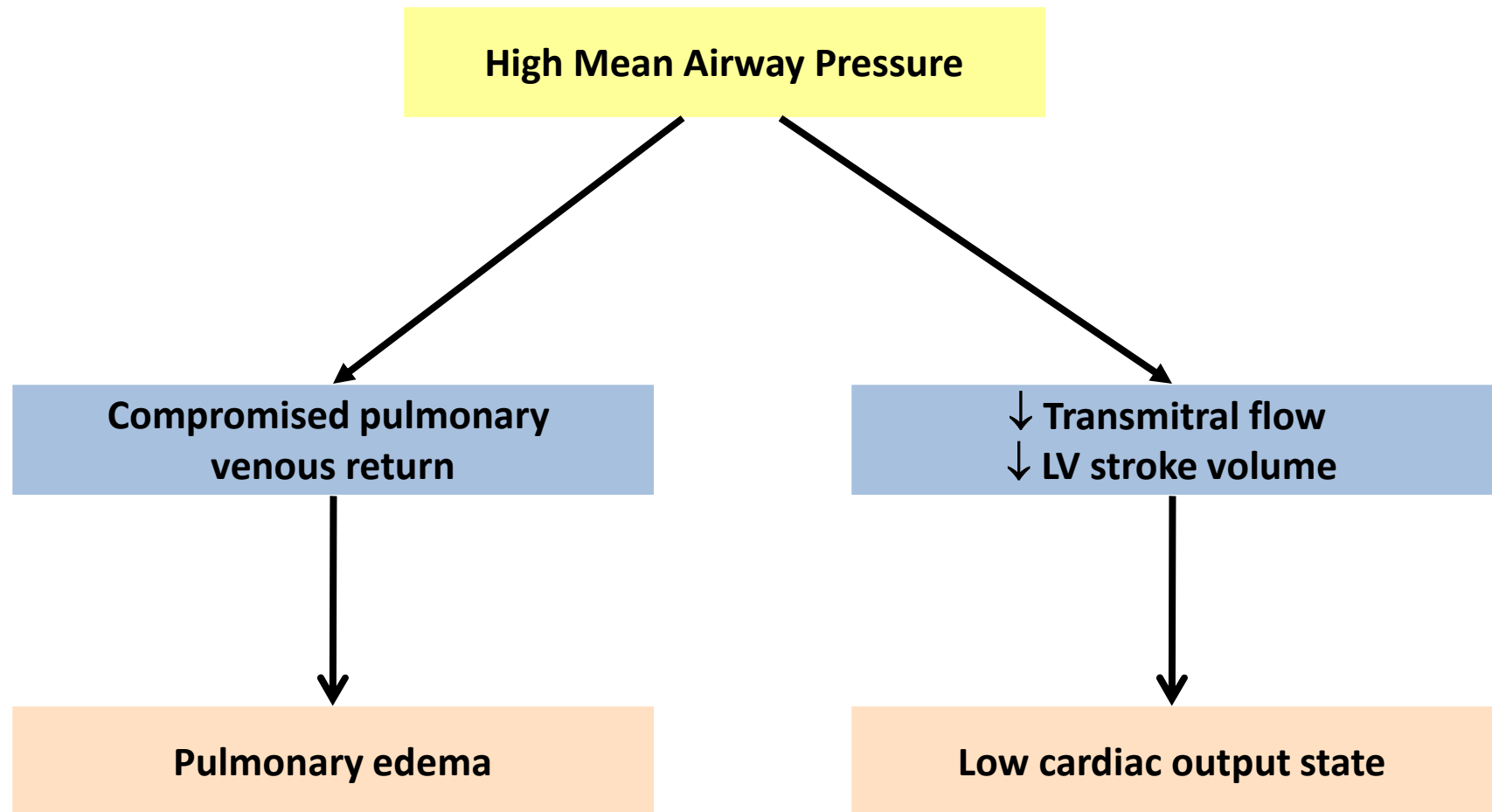
Figure 1 Effects on individual LVO of changes from CV to HFO at T1, and from HFO to CV at T2.

Laubscher 1996 Arch Dis Child

Right Heart Compromise



Left Heart Compromise



Cardiotropic Drugs in PPHN?



Physiologic Considerations:

- Impaired RV contractility and ↓ pulmonary blood flow
- Pressure loaded RV
- Compromised left heart preload and low cardiac output
- Hypercontractile LV

Which Inotrope you start 1st in PPHN ?

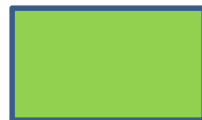
Dopamine



Dobutamine



Milrinone



Goal is maintenance of effective tissue perfusion

- Target normal systolic and diastolic blood pressures
- Ensure adequate cardiac output state (urinary output, pH, lactate)

**Dobutamine is preferable for neonates with
hypotension
and signs of a
low cardiac output (RV or LV) state**

- **Cardiotropic agents:**

Inodilators – *milrinone, dobutamine*

Vasopressors – *dopamine, epinephrine,
vasopressin*

Case : Baby S

Resuscitation:

- HR 20 /min
- No respiratory efforts
- Intubated with ET no 3.5 suction through ET done
- No meconium sucked through ET
- CPR done
- Adrenalin with 0.1ml /kg 1:10,000 given 1st dose through ET
- Did not respond so UVC was put in
- CPR continued for 5 mins
- 2 more doses of Adrenalin was given through UVC and the 3rd dose was 0.2 ml/kg 1:10,000
- With the 3rd dose NS bolus of 10ml/kg stat and 1ml/kg of NaHCO₃ was given through UVC

NICU course

- When reached unit
- Conventional ventilator
- Settings:
 - AC mode
 - PIP started 20 and increased to 28
 - PEEP started 6 increased to 8
 - Ti 0.36secs RR-40 /min
 - End up with PIP/PEEP- 28/8 -----MAP 13
 - FiO2 100%
- Vitals:
 - HR 130/min
 - RR 40 (20 self breaths)
 - **NBP 30/18 (22)**
 - SPO2 : **Rt hand 78% and Rt. Leg 56%**
 - Temp: 36.4 degree

NICU course

- **When examined:**

- Poor tone
- AF at level
- Pupils mid dilated sluggish to react
- Pulses weak in all the 4 limbs
- S1S2 heard , no murmur and S2 loud
- Abdomen was distended with Liver 5-6 cm below right costal margin
- Chest was clear no added sounds

- **Investigations:**

- ABG (40 mins)- pH- 6.66, PaCO₂- 41.4, PaO₂- 75.5, HCO₃⁻- 4.5, BE(-31.4)

Severe Metabolic acidosis

NICU course

- Investigations:
 - Lactate 145 (↑↑)
 - CBC: Hb- 12.6, WBC- 41,400, Plt- 1.09 lac
 - Serum calcium total 7.8
 - CXR
 - Ab US- Hepatomegaly with mild Ascites
 - HUS -- normal



NICU course...Baby S

- She was shifted to HFOV (Sensor medics 3100 A)
- Settings of Ti 33%, MAP 14, Amplitude 30, FiO2 100%
- 1 hr after :
 - ABG: pH- 7.072, PaCO2- 32.7, PaO2- 29.9, HCO3 – 4.5, BE(-19.3)
 - Metabolic acidosis with CO2 wash out
- OI- 34.4
- Lactate – 121(↑)
- **Q: What Next, you have everything in the world?**
Nitric Oxide (iNO)

- **iNO** started at the dose of 20ppm and then weaned off in the next 17 hrs as per the unit protocol

- **CXR** – shows better opened lung fields and cardiac size reduced

- **ABG:** 3hrs post iNO:
pH-7.284, PaCO₂- 29.3, PaO₂- 99.6, HCO₃- 13.6, BE(-11.8)

- Lactate: 57

- MAP – 9

- OI- 3.6

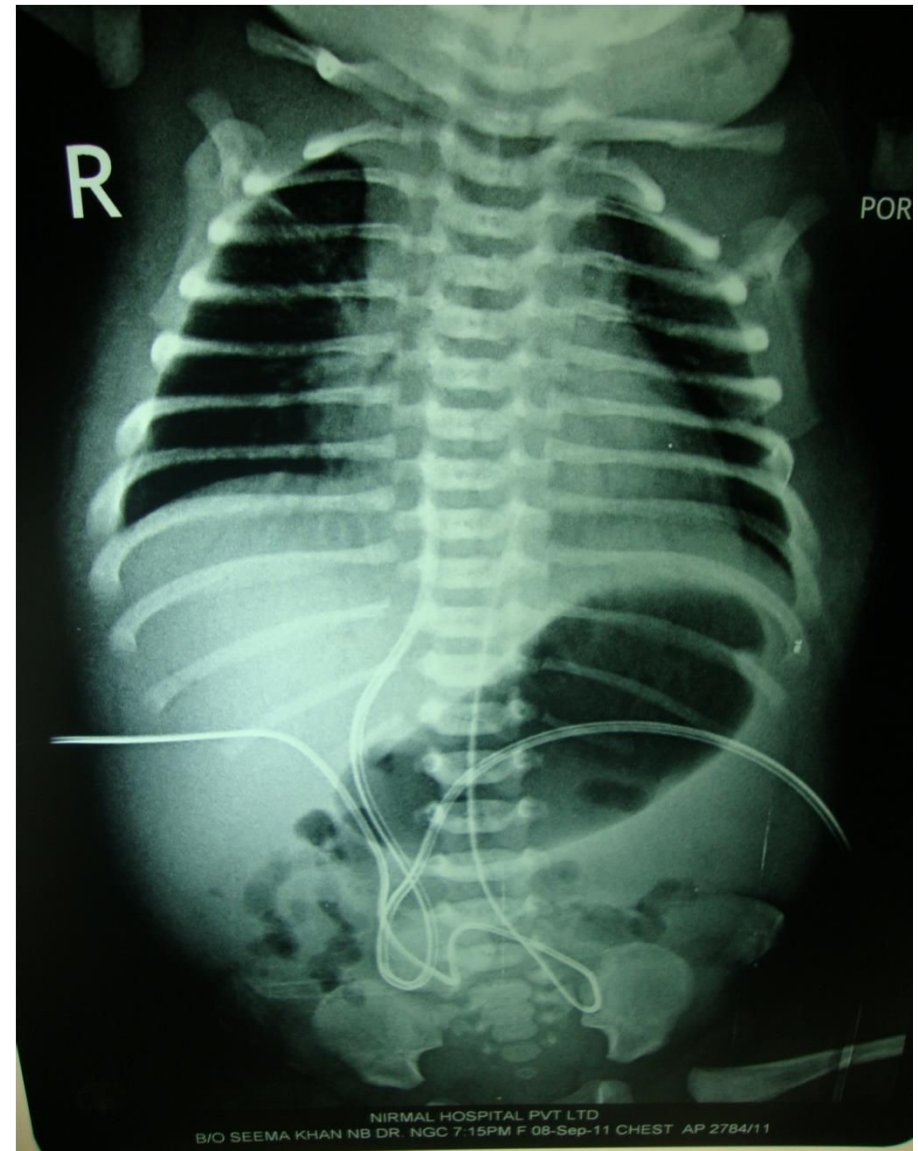
Q: What parameters you will change on HFOV?

- Decrease Amplitude

- Decrease FiO₂

- Wean MAP

One at a time please



Intervention Time(hrs)	40 mins CMV	6 hrs CMV	6.5 hrs HFOV & iNO	9 hrs iNO& HFOV	30 hrs CMV	42 hrs Extubated	42 hrs CPAP
pH	6.66	7.072		7.284	7.299		7.278
PaCO2	41.4	32.7		29.3	26.8		35.7
PaO2	75.5	29.9		99.6	98.1		83.5
HCO3	4.5	9.4		13.6	12.9		16.3
BE	-31.4	-19.3		-11.8	-12.1		-9.5
Lactate	145	121		57	-----		-----
MAP	10	10.3	14	9	8		-----
OI	13.2	34.4		3.6	3		-----

Treatment

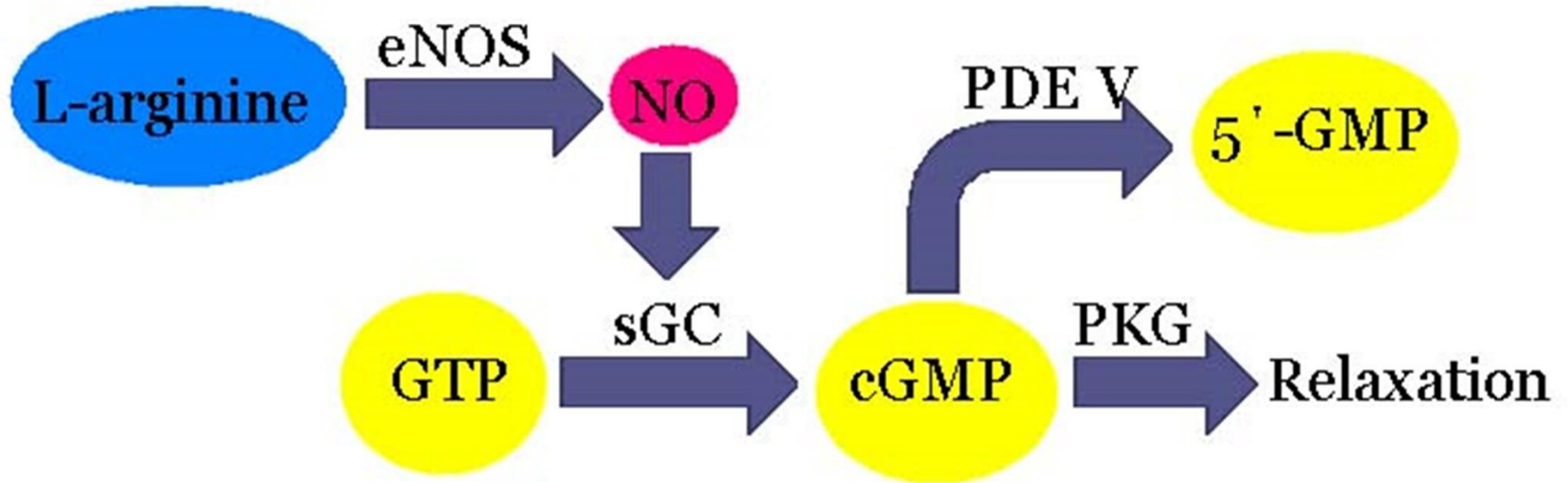
**Gold standard treatment—
iNO**

**Adjunctive Pulmonary vasodilation
therapy –**

Milrinone, Sildenafil, Vasopressin etc.



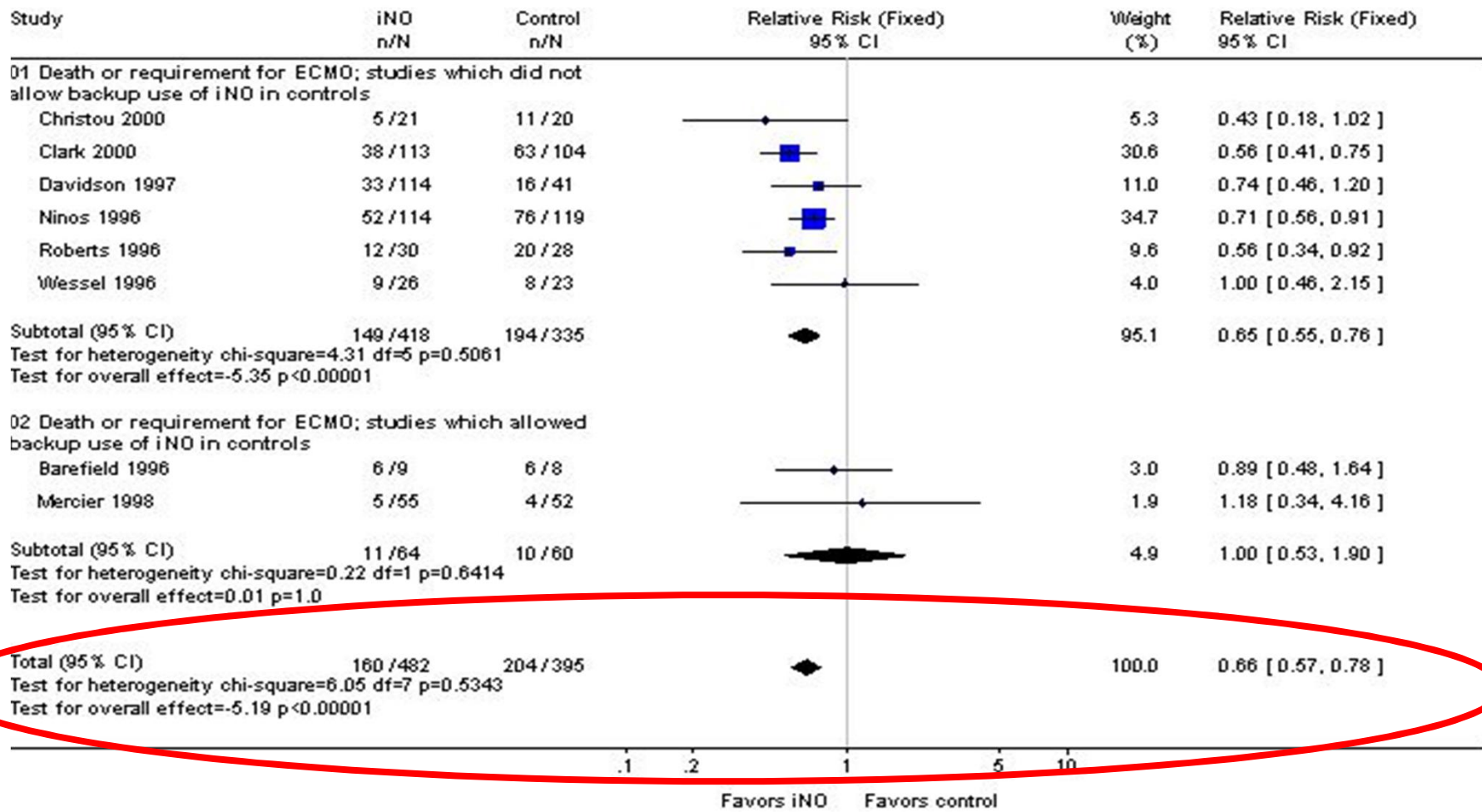
Inhaled Nitric Oxide



- Selective pulmonary vasodilation
- Bronchodilator activity
- Surfactant stimulation

iNO and Death/ECMO

Review: Nitric oxide for respiratory failure in infants born at or near term
 Comparison: 01 Inhaled iNO versus control
 Outcome: 01 Death or requirement for ECMO



Author	Population	Dose	Time	Intermed. outcomes	CLD	CNS
Kinsella 1999 (n=80)	<34 wks a : A < 0.22	5 ppm	D 0-7	↑ a:A ratio	↔	↔
Schrieber 2003 (n=207)	<34 wks < 3 d	10 ppm 5 ppm	D 1 D 1-7	N/A	↓	↓ severe IVH/PVL
Van Meurs 2005 (n=420)	< 34 wks OI > 10	5-10 ppm	D 0-3	N/A	↔ >1kg: ↓	↔ < 1kg: ↑
Hascoet 2005 (n=415)	<34 wks a : A < 0.22	5 ppm	clin	a:A response 45%	↔	↔
Mestan 2005	<34 wks < 3 d	10 ppm 5 ppm	D 1 D 1-7	N/A	↓	↓ delay & disability
Ballard 2006 (n=582)	< 32 wks < 1250 g	20 ppm → 10, 5, 2	D7-21	↓ O ₂ duration Early disch.	↓	↔
Kinsella 2006 (n= 793)	< 34 wks < 48 hrs old 500-1250g	5ppm	D1-21	N/A	↔	↓ 750-999g

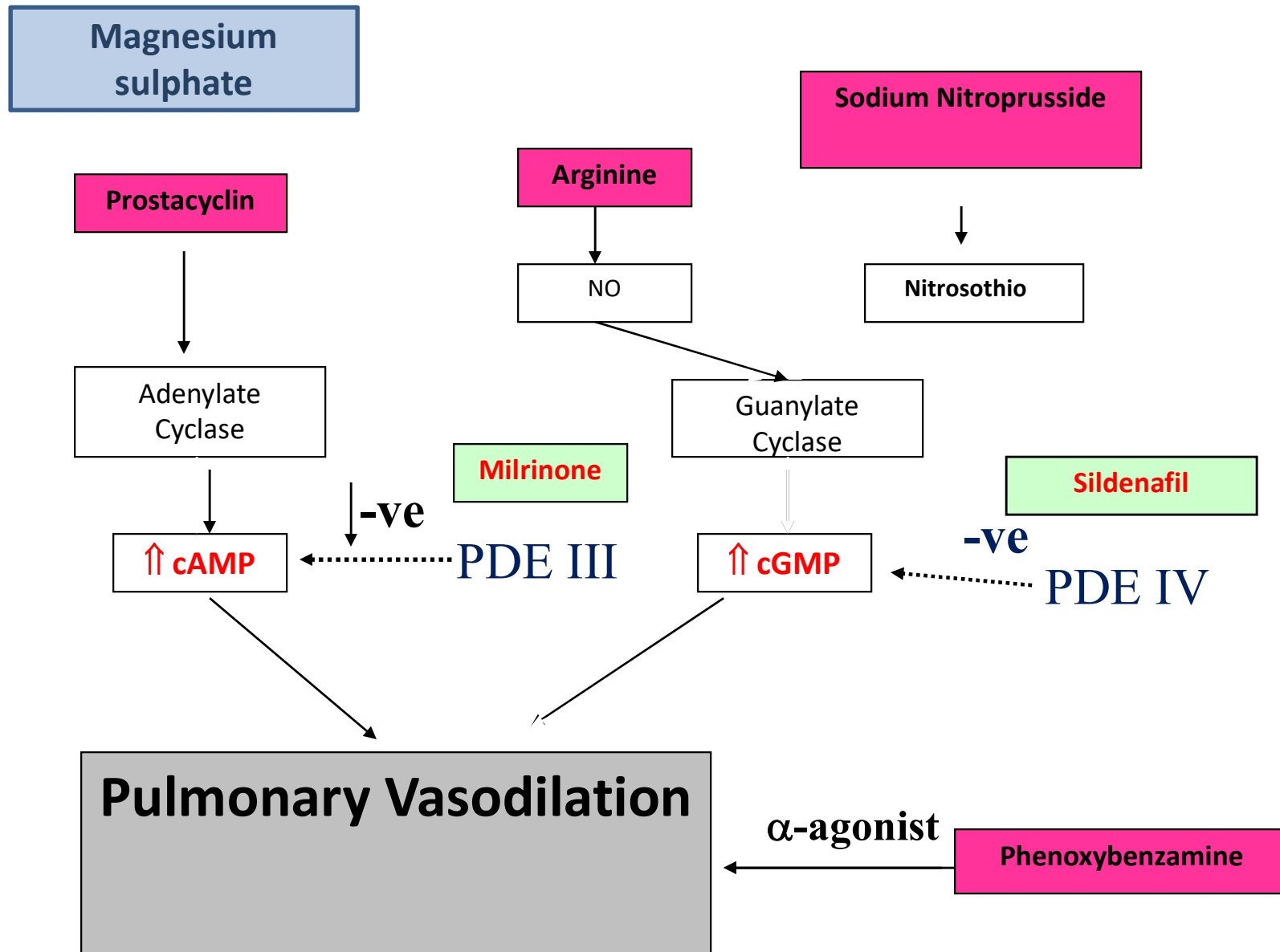
Need for Adjunctive therapy

- 30-40% patients iNO non-responders

NINOS 1997 NEJM

- Escalating costs of iNO treatment
- *Short* (peroxynitrate generation) & *long-term* (altered DNA structure) side effects of iNO treatment
- Role in Preterms

Other Pulmonary Vasodilators



Other Pulmonary Vasodilators

Pulmonary Hypertension and Right Ventricular Dysfunction in Growth-Restricted, Extremely Low Birth Weight Neonates

Olivier Danhaive, MD

Renée Margossian, MD

Tal Geva, MD

Stella Kourembanas, MD

hypotensive episode. The echocardiograms, performed during the acute episode as part of the work-up, showed severe pulmonary hypertension and right ventricle (RV) dysfunction. The goals of this report are to describe the clinical and hemodynamic features of these patients, and to discuss the pathophysiology and the

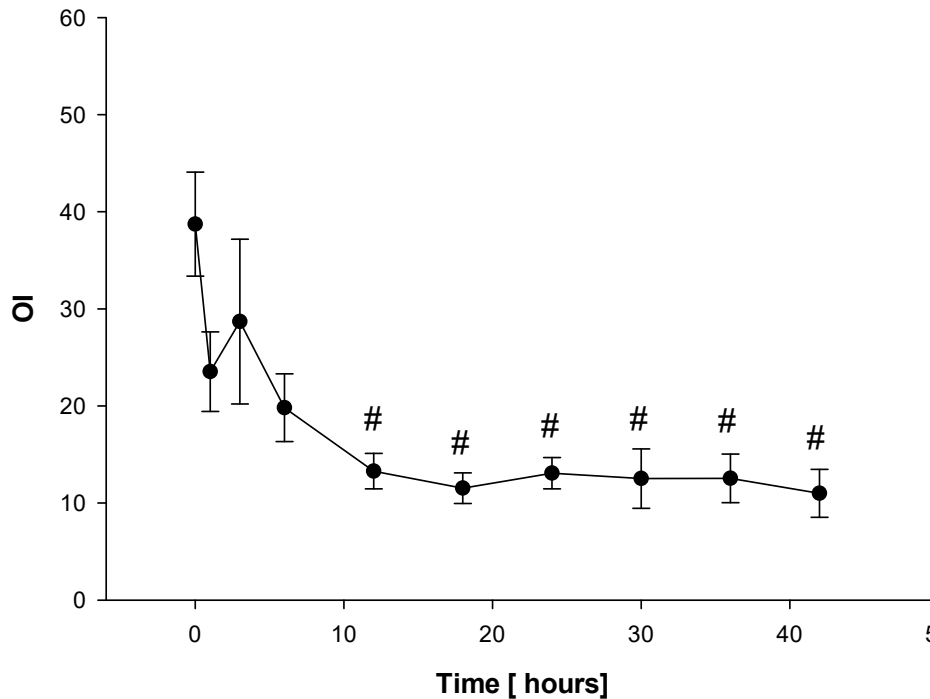
Neonatal Persistent Pulmonary Hypertension Treated with Milrinone: Four Case Reports

Dirk Bassler^a Karen Choong^a Patrick McNamara^c Haresh Kirpalani^{a, b}

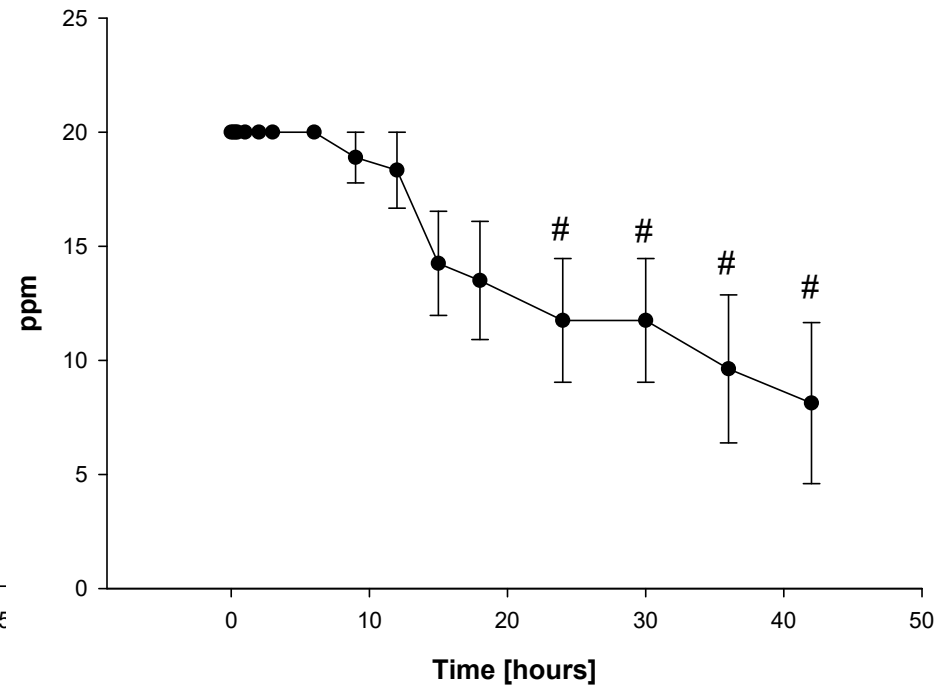
^aDivision of Neonatology, Department of Paediatrics, and ^bDepartment of Clinical Epidemiology, McMaster University Medical Centre, Hamilton, Ont.; ^cDivision of Neonatology, Department of Paediatrics, Hospital for Sick Children, Toronto, Ont., Canada

Milrinone - Oxygenation

Oxygenation index



inhaled Nitric Oxide



- \downarrow FiO_2 , MAP and \uparrow pO_2
- \downarrow base deficit & \downarrow lactate

Sahni M et al, PAS 2010.

Take Home



- PPHN is about elevated PVR and impaired myocardial performance
- Consider impact of oxygen and mechanical ventilation keep SpO_2 88- 95% avoid hyperoxia
- Consider tolerating postductal $SpO_2 > 75\%$
- Avoid hyperventilation , CO_2 wash out for creating Alkalosis

Take Home



- Avoid Sodabcarb therapy
- iNO is an effective pulmonary vasodilator but issues related to toxicity, lack of response , lack of free availability
- Evidence for Adjunctive therapy (milrinone / sildenafil) promising
- Consider cardiotropic support to optimize cardiac output (but not to induce systemic hypertension or raise postductal SpO₂)
- Avoid vasoconstricting agents that increased pulmonary vascular resistance

Thanks